09/673221

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

To:

GILES, Ashley, Simon
Haseltine Lake & Co.
Imperial House
15-19 Kingsway
London WC2B 6UD
ROYAUME-UNI

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

Date of mailing (day/month/year) 30 October 2000 (30.10.00)	
Applicant's or agent's file reference HL55622/001/MRJ	**IMPORTANT NOTIFICATION**
International application No. PCT/GB99/01138	**International filing date** (day/month/year) 14 April 1999 (14.04.99)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
STOWIC RESOURCES LIMITED Ross House Stow-On-The-Wold Gloucesthershire GL54 1AF United Kingdom	GB	GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
STOWIC RESOURCES LIMITED Ross House Stow-On-The-Wold Gloucestershire GL54 1AF United Kingdom	GB	GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Christine Carrié
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

003620376

PATENT COOPERATION TREATY

RIA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 December 1999 (09.12.99)	
International application No. PCT/GB99/01138	**Applicant's or agent's file reference** HL55622/001/MRJ
International filing date (day/month/year) 14 April 1999 (14.04.99)	**Priority date** (day/month/year) 14 April 1998 (14.04.98)
Applicant TUCKER, Mark, Rupert	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

12 November 1999 (12.11.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer J.M. Vivet
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
HL55622/001 MRJ		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 99/ 01138	14/04/1999	14/04/1998
Applicant		
STOWIC RESOURCES LIMITED.et.al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

[X] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01138

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/70 B65B9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K B65B B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 614 076 A (RATHEMACHER JOHN W) 30 September 1986 (1986-09-30) claims; figures 1,2,6,7	
A	US 4 845 926 A (DAVIS STEVEN D) 11 July 1989 (1989-07-11) column 3, line 42 - column 4, line 2 claims 12-16; figures 1-3	
A	US 4 004 399 A (BORRELLO DENIS) 25 January 1977 (1977-01-25) column 6, line 8 - line 12 claims 1-12; figures 2,4	

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 July 1999	20/07/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Epskamp, S

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01138

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 210 908 A (SAMBERG MICHAEL) 12 October 1965 (1965-10-12) column 1, line 27 - line 46 column 4, line 46 - line 51 claims 1-5; figures 1-4	
A	FR 1 068 961 A (WASSILIEF VICTOR) 2 July 1954 (1954-07-02) column 1, line 36 - column 2, line 7 column 6, line 11 - line 15 claims; figures	
A	US 4 769 974 A (DAVIS STEVEN D) 13 September 1988 (1988-09-13) claims; figures	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/01138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4614076 A	30-09-1986	CA 1266426 A,C	06-03-1990
		EP 0202391 A	26-11-1986
US 4845926 A	11-07-1989	US 4769974 A	13-09-1988
		US 4768330 A	06-09-1988
US 4004399 A	25-01-1977	DE 2610513 A	23-09-1976
		FR 2303712 A	08-10-1976
		GB 1508704 A	26-04-1978
		JP 1051984 C	26-06-1981
		JP 51116785 A	14-10-1976
		JP 55043963 B	10-11-1980
		US 4067173 A	10-01-1978
US 3210908 A	12-10-1965	NONE	
FR 1068961 A	02-07-1954	NONE	
US 4769974 A	13-09-1988	US 4845926 A	11-07-1989

the
ERNATIONAL PRELIMINARY EXAMINING AUTHORITY

JONES, M.R. et al.
HASELTINE LAKE & CO.
Imperial House
15-19 Kingsway
London WC2B 6UD
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	15.02.2000
Applicant's or agent's file reference: HL55622/001 MRJ	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/01138	14/04/1999	14/04/1998

Applicant
STOWIC RESOURCES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international applicati

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communicatk to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of t report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Articl 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation mu contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Tantum, P Tel.+49 89 2399-8730

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
HL55622/001 MRJ		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/01138	14/04/1999	14/04/1998

International Patent Classification (IPC) or national classification and IPC
A61K9/70

Applicant
STOWIC RESOURCES LIMITED et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report
   II ☐ Priority
   III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☐ Lack of unity of invention
   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12/11/1999	15.02.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lindner, A Telephone No. +49 89 2399 8640

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01138

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-12 as originally filed

Claims, No.:

1-19 as originally filed

Drawings, sheets:

1/1 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 19.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 19 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

see separate sheet

III:

Claim 19 is not clear, as it refers to the drawings. As a consequence, claim 19 is not considered in this report.

V:

1. Reference is made to the following document:

   D1 = US-A-4 614 076

2. D1 discloses a continuous process for the preparation of transdermal patches comprising the feeding of a strip of disposable, adhesive and permeable layers and of a second strip of an impermeable backing layer onto which a medicament had been deposited and sealing the strips in the nip of two heated crimp rolls, thus forming multiple patches side by side simultaneously. D1 does not specifically relate to a first and a second sealing station nor is the liquid containing the active agent filled into the pouch formed by sealing three sides of the strips. As a consequence, the requirements of article 33(2) PCT.

3. In view of the numerous differences in the process steps, D1 is not pertinent for inventive step. The other documents cited in the search report do not concern the preparation of transdermal patches and are therefore not relevant, either. The subject-matter of claims 1-18 therefore involves an inventive step (article 33(3) PCT).

M·H

17

PATENT COOPERATION TREATY

PCT

REC'D 17 FEB 2000

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
HL55622/001 MRJ		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB99/01138	14/04/1999	14/04/1998
International Patent Classification (IPC) or national classification and IPC A61K9/70		
Applicant STOWIC RESOURCES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12/11/1999	15.02.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lindner, A Telephone No. +49 89 2399 8640

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01138

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-12 as originally filed

Claims, No.:

1-19 as originally filed

Drawings, sheets:

1/1 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 19.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 19 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

see separate sheet

III:

Claim 19 is not clear, as it refers to the drawings. As a consequence, claim 19 is not considered in this report.

V:

1. Reference is made to the following document:

   D1 = US-A-4 614 076

2. D1 discloses a continuous process for the preparation of transdermal patches comprising the feeding of a strip of disposable, adhesive and permeable layers and of a second strip of an impermeable backing layer onto which a medicament had been deposited and sealing the strips in the nip of two heated crimp rolls, thus forming multiple patches side by side simultaneously. D1 does not specifically relate to a first and a second sealing station nor is the liquid containing the active agent filled into the pouch formed by sealing three sides of the strips. As a consequence, the requirements of article 33(2) PCT.

3. In view of the numerous differences in the process steps, D1 is not pertinent for inventive step. The other documents cited in the search report do not concern the preparation of transdermal patches and are therefore not relevant, either. The subject-matter of claims 1-18 therefore involves an inventive step (article 33(3) PCT).

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 9/70, B65B 9/02

A1

(11) International Publication Number: **WO 99/52513**

(43) International Publication Date: 21 October 1999 (21.10.99)

(21) International Application Number: PCT/GB99/01138

(22) International Filing Date: 14 April 1999 (14.04.99)

(30) Priority Data:
9807917.1 14 April 1998 (14.04.98) GB

(71) Applicant *(for all designated States except US)*: STOWIC RESOURCES LIMITED [GB/GB]; Ross House, Stow-On-The-Wold, Gloucesthershire GL54 1AF (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: TUCKER, Mark, Rupert [GB/GB]; 35 Bliss Mill, Chipping Norton, Oxon OX7 5JR (GB).

(74) Agent: GILES, Ashley, Simon; Haseltine Lake & Co., Imperial House, 15-19 Kingsway, London WC2B 6UD (GB).

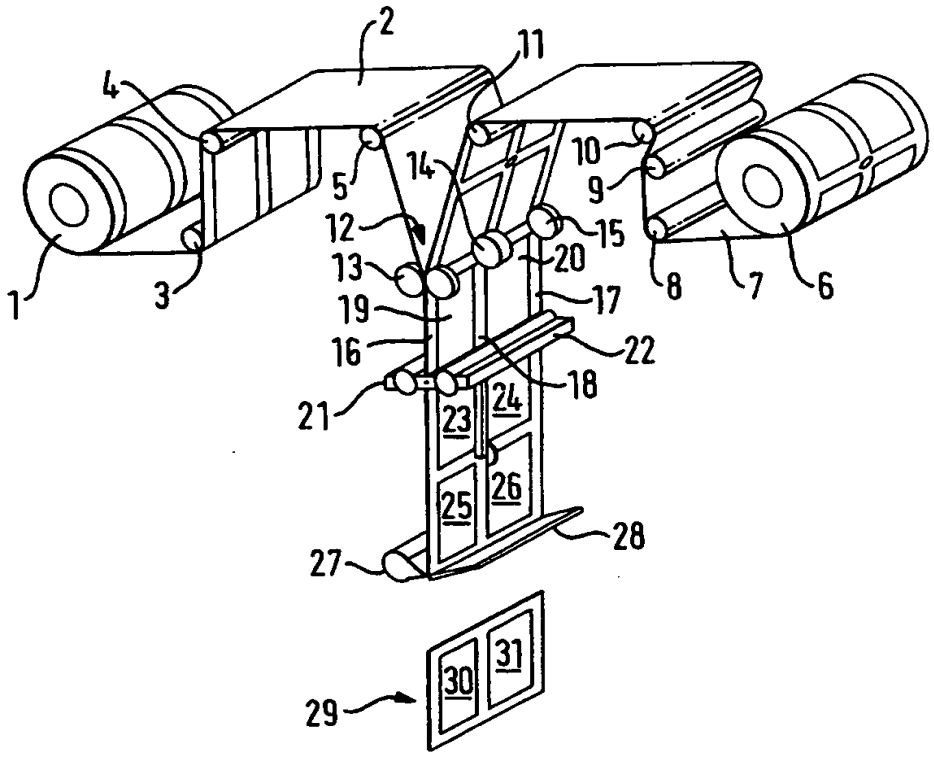
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: METHOD OF MANUFACTURING TRANSDERMAL PATCHES

(57) Abstract

A continuous process for forming a transdermal patch which comprises the steps of: continously feeding a strip of material comprising a layer of permeable membrane; continuously feeding into close proximity and in face-to-face relationship with the first strip a second strip formed of impermeable backing material; passing the first and second strips together through a filling and sealing station in which the material containing an active substance is introduced between the strips and pouches are formed by first sealing devices which seal the strips together in a longitudinal direction of the strips and second sealing devices which seal the strips together in a transverse direction of the strips; the size of the pouches being adjusted by adjusting the number position and/or frequency of operation of the first sealing devices and/or by adjusting the number position and/or frequency of operation of the second sealing devices.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

METHOD OF MANUFACTURING TRANSDERMAL PATCHES

This invention relates to a method of manufacturing transdermal patches, for example the so-called nicotine patches which can be applied to the skin of a person who wishes to receive some nicotine whilst giving up smoking.

One particularly satisfactory form of patch is disclosed in United Kingdom Patent Specification No. 2232892, where it is broadly defined as an occlusive body for the transdermal administration of a physiologically active substance, the body comprising an impermeable backing and a microporous or permeable membrane which define a cavity therebetween, said physiologically active substance being contained within said cavity in liquid form, said microporous or permeable membrane being permeable to and in contact with said physiologically active substance and the liquid material confined between said impermeable backing and said microporous or permeable membrane within said cavity being substantially immobilised by a viscous flowable gel, characterised in that either;

a) said membrane is hydrophilic and the contents of said cavity are hydrophobic; or

b) said membrane is hydrophobic and said cavity contains a hydrophilic wetting agent;

whereby, in use, passage of said physiologically active substance through said microporous membrane is rate-controlling and said physiologically active substance is released from said microporous membrane at a rate that is substantially constant over a period of hours.

Typically the occlusive body in the form of the patch has, in going from one side to the other, several layers which may include: (i) a disposable, removable protective layer, (ii) a layer of adhesive, (iii) the permeable membrane or membranes, (iv) a layer of gel

containing the physiologically active substance (such as nicotine), and (v) the layer of an impermeable backing material.

In practice the first three (or more) layers may be employed as a pre-formed laminate. It is then necessary to apply the active substance (layer (iv)) to the laminate (to the combination of layers (i) to (iii)) and then to secure the active substance in place by providing the backing layer (layer (v)).

Typically when manufacturing a product of this nature, the materials are fed horizontally and a discrete amount of the active substance is deposited at a fixed interval, or station, along the laminate, with the backing material then being brought into position in order to cover the active substance prior to the backing material being secured, for example by sealing, to the laminate in regions around the discrete amounts of active substance. The process is non-continuous and known as 'form, fill, seal' such as is demonstrated by a blister packer. It requires substantial re-tooling if volumetric changes to the reservoir are desired.

Bearing in mind that the active substance is normally present in a gel, it can be appreciated that there are considerable handling problems associated with providing the appropriate amounts of the gel at neatly spaced intervals along the laminate without the gel being exposed to the environment. Moreover, when it is wished to vary the volume of the gel, so as to vary the amount of active substance in the patch, or to vary the skin contact area of the product, (assuming that the concentration of active substance in the gel remains the same), it can be difficult to alter the machine whilst in operation so that the desired effect is achieved.

Equipment already exists for wrapping items such

as so-called telephone cards, which are cards for insertion into a telephone machine to allow the user to use the telephone for the duration of the unused units electromagnetically held in the telephone card. In such equipment a first layer of material is caused to travel vertically downwards close to, and parallel to, a second layer of material. Often one layer is transparent and the other is opaque and contains instructions and other information. The two layers of material are brought together and are sealed to each other by opposing pairs of sealing devices, e.g. heated wheels, which act on the opposing longitudinal edges of the two strips of material being brought together. In addition, an intermittent sealing mechanism acts transversely across the juxtaposed layers already joined at their opposing longitudinal edge regions, so that a pouch results. As the pouch is being formed a telephone card, or the like, is fed into the pouch which still remains open along its upper (fourth) edge. Once the card or other item is correctly located in the pouch, and while both layers continue to move downwardly, the fourth open edge of the pouch is closed, typically by the same horizontal sealing mechanism. In fact, the most efficient way of achieving this is for the upper edge of a lower pouch to be sealed at the same time as the lower edge of the immediately upper pouch is being sealed. Both sealing operations can be carried out simultaneously by the same sealing arrangement.

If desired at about the same time as the sealing is being effected to form the last transverse seal, or immediately downstream thereof or at a much later stage, the pouches can be separated from each other by cutting, or else a line of weakness can be formed in the region between the upper seal of the lower pouch and the lower seal of the upper pouch so that the

pouches are still joined in end to end relationship but with a line of weakness which can readily be ruptured.

Somewhat similar equipment can also be used for creating pouches containing other products, such as sugar or sauces (for use in restaurants).

According to a first aspect of the present invention, there is provided a method of forming a transdermal patch, which comprises the steps of:

feeding at a first linear speed a strip of materials comprising a disposable layer, a layer of adhesive and a layer of a permeable membrane;

feeding into close proximity and in face-to-face relationship with the first strip at least one second strip formed of impermeable backing material(s), at the same first linear speed;

passing the first and second strips together through a first sealing station at which at least the opposed longitudinal edge regions of the strips are secured together, optionally with intermediate regions of the strips being secured along their lengths, so as to form at least one elongate chamber;

passing the first and second strips joined at least at their longitudinal edges, through a second sealing station at which the strips are sealed to each other transversely at intervals along the strips, whereby the or each chamber becomes an open-topped pouch;

introducing a liquid containing an active substance into the pouch or pouches, once formed; and

sealing the pouches along their previously open edges so as to form completely sealed pouches.

According to a second aspect of the present invention there is provided a continuous process for forming a transdermal patch which comprises the steps

of:

continously feeding a strip of material comprising a layer of permeable membrane;

continously feeding into close proximity and in face-to-face relationship with the first strip a second strip comprising an impermeable backing material;

passing the first and second strips together through one or more filling and sealing stations in which the material containing an active substance is introduced between the strips and pouches are formed by first sealing devices which seal the strips together in a longitudinal direction of the strips and second sealing devices which seal the strips together in a transverse direction of the strips;

the size of the pouches being adjusted by adjusting the number position and/or frequency of operation of the first sealing devices and/or by adjusting the number position and/or frequency of operation of the second sealing devices.

The process is continuous as a result of the dosing and patch formation happening in a synchronised/simultaneous manner. This is distinct from the blister technique which is a station-by-station function and non-continuous.

Conveniently, at the second sealing station the upper previously open region of a pouch or pouches is sealed and the sealing simultaneously closes the bottom of the pouch or pouches immediately above the first mentioned pouch or pouches.

The method can also include a separation cutting step, in which a transverse cutting exercise takes place so as to separate one sealed pouch containing the active substance from the adjacent pouches upstream and downstream.

If a tear-tab at one corner of the patch is required, a suitable "kiss-cut" function can be

provided at this stage. In addition, other functions such as registration, embossing and de-bossing, can be performed at, or immediately after, this stage.

In addition, when the two strips are first brought together and sealed along their longitudinal edges and when there is one or more additional longitudinal seal being created intermediate the edge region seals, then there will be two or more pouches being created, and it is desirable to separate those laterally adjacent pouches at a suitable downstream station. This can be achieved by, for example, rollers acting on opposite sides of the joined strips with at least one of the rollers having a cutting edge so as to separate laterally adjacent pouches.

Preferably, when effecting the method of the present invention, a gas flushing system is employed, which can be achieved by placing a small bore tube adjacent the liquid (gel) delivery tube, which ensures that the pouch will, when sealed, effectively only contain the gel itself and the flushing gas, for example nitrogen. Alternatively, instead of employing an inert flushing gas, the filling and sealing can be effected in a "vacuum".

The sealing of the adjacent strips can be effected by opposing pairs of sealing devices (e.g. heated rollers), and the means by which the liquid (gel) containing the active substance is introduced can take the form of a tube the lower, open end of which can be at a level considerably below the axes of rotation of those sealing devices, and can be positioned at a level just above where the transverse sealers are employed which come together intermittently to provide the transverse seals across the strips at the desired spaced intervals. It will be appreciated that careful synchronisation of the different pieces of equipment which carry out the sealing and cutting steps is

required, but existing technology is readily available for this.

When it is desired to increase the active amount of substance, whilst retaining the concentration of the active substance constant in the gel, it is clearly necessary to provide a larger volume of the gel. In order to accommodate the larger volume, the pouch needs to be larger and this can be achieved in one or more ways. If, for instance, during pouch production three pouches are being produced side by side, it is possible to reduce the number of pouches to two which will increase the available width of each pouch. This is done by removing one of the pairs of sealing devices (e.g. heating rollers) and adjusting the location of the remaining intermediate pair of sealing devices; moreover, one of the dosing nozzles is removed.

Alternatively, or in addition, the timing of the transverse sealing is adjusted to take place at longer intervals with the result that longer pouches are formed.

Obviously, when the transverse sealing is less frequent during the formation of the longer pouches, it is also necessary that there is corresponding adjustment to the transverse cutting equipment so that the cutting remains along the seal which separates one sealed pouch or row of pouches from the adjacent pouch or row of pouches.

It is to be appreciated that, even when the volume of the pouch is being altered, it is possible to continue to feed in the first and second strips at the same linear feed speed. Furthermore, the two or more in-feed rolls of material do not need to be changed as part of the retooling exercise common in other manufacturing methods. In other words, the same materials and some rolls can be used without adjustment to obtain a different pouch size. In fact, it is a

great advantage of the present invention that variation in the volume of the pouch desired does not necessitate any alteration to the components responsible for feeding in the two starting strips of material. The handling of such strips is a delicate matter and it is therefore of considerable advantage to maintain the feed speeds at a constant. This is because continuous processes exert a constant pressure/strain on the materials resulting in less damage and/or distortion of the final product and a "flatter" more aesthetically pleasing pouch than intermittent ones. Indeed, intermittent or non-continuous processes such as blister packers have a stop-start motion that can cause damage by stretching the material.

It is a relatively simple matter, through the appropriate control equipment, to cause the transverse sealing components to operate at longer or shorter intervals so as to produce longer or shorter pouches, and equally it is relatively simple for the same control equipment to coordinate the components responsible for the transverse cutting without re-tooling the machine.

It has been found by experiment that the process according to the present invention can be used to manufacture pouches as small as $2cm^2$. This contrasts with the prior art processes in which a minimum pouch size of no less than $5cm^2$ was possible.

The tube or tubes, or like, responsible for injecting the gel containing the active substance into the pouches remains in the same position and injects the appropriate volume of gel into the pouch as the transverse seal is being formed or immediately after it has been formed. Accurate dosing equipment is available to ensure that precisely the desired amount of gel is deposited into each pouch and can be adjusted to compensate for an increase, or decrease, in the

volumetric requirements of the pouch in a similar way to the timing adjustment of the sealing devices.

Preferably, the materials are fed through the stations in a substantially vertical direction and the liquid containing an active ingredient is introduced into the pouch or pouches in a substantially vertical direction. However, alternatively the materials may be fed through the stations in a substantially horizontal direction whilst the liquid is still introduced in a substantially vertical direction.

For a better understanding of the present invention, and to show how the same may be carried into effect, reference will now be made, by way of example, to the accompanying drawing, which shows a perspective view of a method in accordance with the present invention being conducted on equipment having the appropriate facilities to effect the method.

In the drawing there are shown a roll 1 of backing material in the form of a strip 2 which is drawn off from the roll 1 and passed around a tensioning roller 3, then over a guide roller 4 and another guide roller 5 and passed further downstream. Somewhat similarly, but starting from the opposite side of the equipment, there is a roll 6 of multi-layer material (of the type mentioned above) with the strip 7 of that material (e.g. in the form of a laminate) being drawn off from the roll 6 and passed around its own tensioning roller 8 and then around three guide rollers 9, 10 and 11 and downstream into the region of a "nip" 12 where it meets the strip 2. The two strips 2 and 7 pass between three pairs of sealing devices in the form of pairs of heated rollers 13, 14 and 15 which have the effect of sealing the strips 2 and 7 at their longitudinally opposing edge regions 16 and 17 and also at a central location 18, so that the region between the two strips 2 and 7 is divided into two pouches 19 and 20 which are open at

their upper and lower ends. However, as those pouches 19 and 20 travel downwardly they encounter the transverse intermittent sealing system which comprises two heated bars 21 and 22 which are generally separated from each other but intermittently are brought together to form a horizontal seal across the downwardly travelling strips 2 and 7 whereby the pouches 19 and 20 are then sealed along their lower edges, as well as their vertical edges. Not shown (for the sake of clarity) are two tubes which project into the pouches 19 and 20 with the lower end regions of the tubes being just above the heated bars 21 and 22. Adjacent those two tubes are two smaller tubes (also not shown) through which an inert gas (particularly nitrogen) under pressure is introduced into the pouches 19 and 20 to create an inert atmosphere during the dosing of the pouches by the introduction of discrete doses of gel through the main tubes into the pouches 19 and 20. When the heated bars 21 and 22 are separated the filled pouches 19 and 20 can move further downward to the position occupied by the pouches 23 and 24. It can readily be seen that the heating and sealing action of the bars 21 and 22 simultaneously seals the lower edges of the pouches 19 and 20 and the upper edges of the pouches 23 and 24. It is also to be appreciated that the strips 2 and 7 when separate and when travelling together move at the same linear speed throughout in a continuous manner. For this reason the bars 21 and 22, when acting on the strips 2 and 7, move at the same speed as those strips so that the smooth progress of those strips is not impaired.

Shown below the pouches 23 and 24 are two further pouches 25 and 26 produced immediately before the production of the pouches 23 and 24. As shown in the drawing, the lower edge of the pouches 25 and 26 is being acted on by cutting devices 27 and 28 which cut

transversely across the combined strips 2 and 7 to separate the pair of pouches 25 and 26 from the pair 29 shown below as pouches 30 and 31.

It can readily be appreciated that comprehensive equipment, such as a bandolier mechanism, can be employed to draw off the strips 2 and 7 at a uniform speed and to feed them into the sealing system consisting of the heated rollers 13, 14 and 15 at the same speed and to pass the united strips 2 and 7 through the sealing system 21, 22 and through the cutting system 27, 28 at the same uniform speed.

If longer pouches are required, it is merely necessary to cause the sealing system 21, 22 to operate for the same duration but at greater intervals and for the cutting system 27, 28 also to operate at correspondingly greater intervals. It will also readily be appreciated that the provision of the three pairs 13, 14 and 15 of heated rollers of the sealing system causes the production of two pouches 19 and 20, and that by increasing or decreasing the number of pairs of heated rollers or other sealing devices there is a corresponding increase or decrease in the number of pouches generated in side-by-side relationship.

The dosing through the tubes (not shown) of the gel containing the active substance (e.g. nicotine) can be effected by sophisticated dosing equipment which is available on the market, for example from the company Hibar Systems Limited.

Although the dosing of the gel through the tube or tubes into the pouch or pouches is effected as intermittent deposits, the supply of the inert gas through the adjacent tube or tubes to create an inert atmosphere in the pouch or pouches being formed can be effected continuously.

With suitable control equipment it will be possible, at the touch of a button, to alter the

location of the heated rollers 13, 14 and 15 thereby varying the width of the pouches and also to alter the frequency of the sealing operation of the heating components 21, 22 and cutting components 27, 28 so as to vary the length of the pouches. No re-tooling is necessary. Thus variation in the magnitude of the pouches can be effected without having to replace any of the components of the equipment by replacement components. All that needs to be varied is the location of the heated rollers 13, 14 and 15 and/or the frequency of operation of the transverse sealing system, 21, 22 and the cutting system 27, 28. If desired, the backing material can be flesh-coloured or clear on that side which is to face outwards when the patch is applied to a person. At further stages downstream, the individual pouches can be cropped to provide a 'kiss-cut' 'tear-tab' and be separately packed in their own individual wrappers and batches of the wrappers collected together in packets or other suitable containers.

CLAIMS

1. A continuous process for forming a transdermal patch, which comprises the steps of:

continuously feeding at a first linear speed a strip of materials comprising a disposable layer, a layer of adhesive and a layer of a permeable membrane;

continously feeding into close proximity and in face-to-face relationship with the first strip at least one second strip formed of impermeable backing material(s), at the same first linear speed;

passing the first and second strips together through a first sealing station at which at least the opposed longitudinal edge regions of the strips are secured together, optionally with intermediate regions of the strips being secured along their lengths, so as to form at least one elongate chamber;

passing the first and second strips joined at least at their longitudinal edges, through a second sealing station at which the strips are sealed to each other transversely at intervals along the strips, whereby the or each chamber becomes an open-topped pouch;

introducing a liquid containing an active substance into the pouch or pouches, once formed; and

sealing the pouches along their previously open edges so as to form completely sealed pouches.

2. A continuous process as claimed in claim 1, in which, at the second sealing station the previously open region of a pouch or pouches is sealed and the sealing simultaneously closes the adjacent region of the pouch or pouches immediately upstream of the first mentioned pouch or pouches.

3. A continuous process as claimed in claim 1 or 2, further including a separation cutting step in which a transverse cutting exercise takes place so as to separate one sealed pouch containing the active

substance from the adjacent pouches upstream and downstream.

4. A continuous process as claimed in any one of the preceding claims, in which a "kiss-cut" function is provided at the separation cutting step.

5. A continuous process as claimed in any one of the preceding claims, in which the two strips are first brought together and sealed along their longitudinal edges and separately or simultaneously one or more additional longitudinal seals are created intermediate the edge region seals thereby creating two or more laterally adjacent pouches across the width of the strips.

6. A continuous process as claimed in claim 5, in which the laterally adjacent pouches are separated in a longitudinal cutting step in which rollers, at least one of which has a cutting edge, act on opposite sides of the join strips, so as to separate the laterally adjacent pouches.

7. A continuous process as claimed in any one of the preceding claims, further comprising a gas flushing step in which the or each pouch is flushed with gas prior to and/or during the step in which liquid is introduced.

8. A continuous process as claimed in claim 7, in which in the gas flushing step, a small bore tube is placed adjacent the liquid delivery tube and flushing gas is ejected from the tube directly into the pouch.

9. A continuous process as claimed in any one of the preceding claims, in which the filling and sealing steps are effected at a pressure lower than atmospheric pressure.

10. A continuous process as claimed in any one of the preceding claims, in which the sealing of adjacent strips is effected by opposing pairs of longitudinal or transverse sealing devices.

11. A continuous process as claimed in claim 10, in which the means by which the liquid containing the active substance is introduced takes the form of a filling tube which is inserted into the or each pouch.

12. A continuous process as claimed in claim 11, in which the lower end of the filling tube is at a level considerably below the axis of rotation of the sealing devices.

13. A continuous process as claimed in claim 10 or 11, in which the filling tube is positioned at a level just above where the transverse sealing devices are disposed.

14. A continuous process as claimed in any one of claims 10 to 13, further comprising the step of adjusting the number of pouches being produced side by side, the step comprising adding or removing one or more pairs of longitudinal sealing devices and adjusting the location of the intermediate sealing devices.

15. A continuous process as claimed in any one of claims 10 to 14, further comprising the step of adjusting the size of the pouches, the step comprising adjusting the timing of transverse sealing devices, thereby changing the length of the pouches.

16. A process as claimed in any one of the preceding claims, in which the size of the pouches is not less than $2cm^2$.

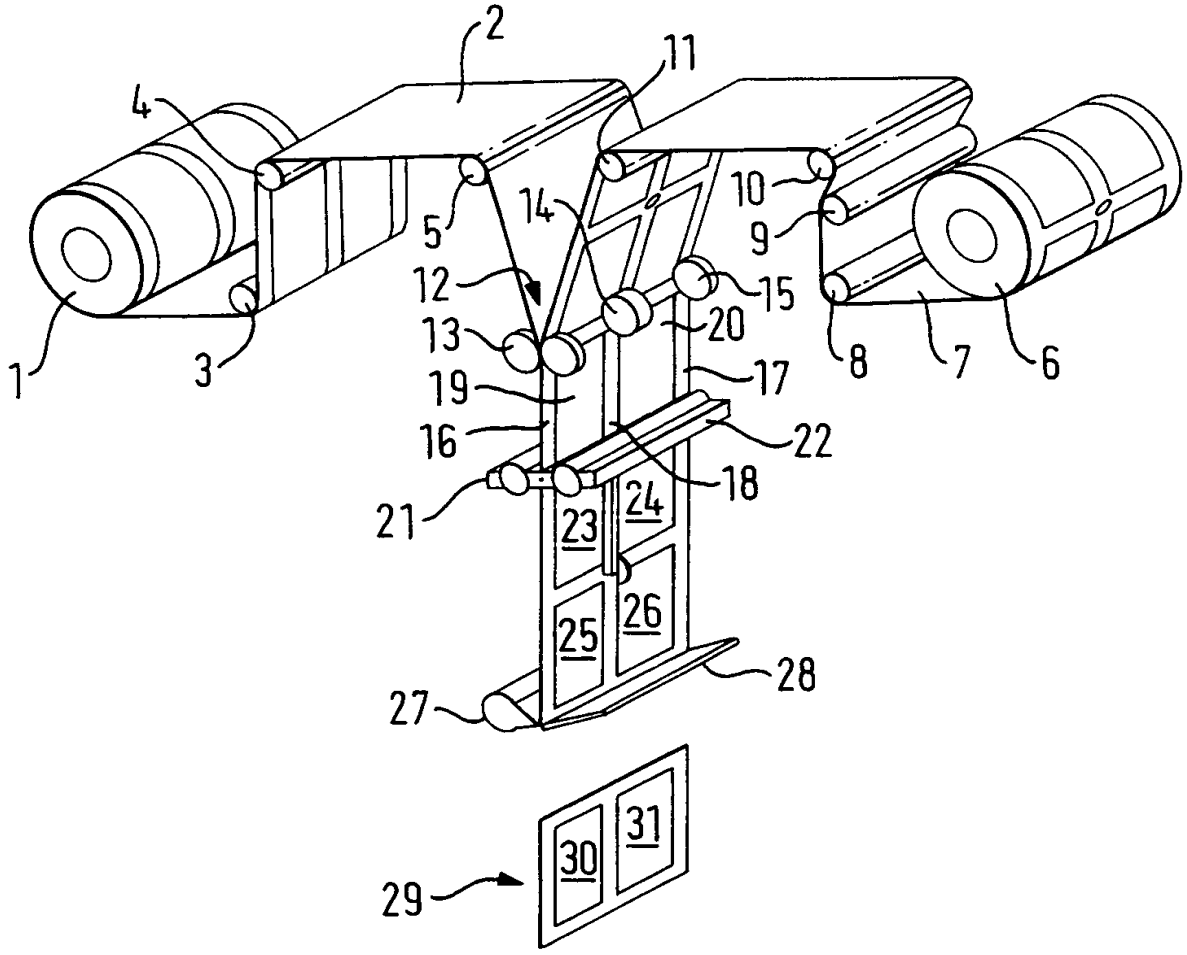
17. A continuos process as claimed in any one of the preceding claims, in which the strips are fed in a substantially vertical direction and the liquid containing an active ingredient is introduced into the pouch or pouches in a substantially vertical direction.

18. A continuous process as claimed in any one of claims 1 to 16, in which the strips are fed in a substantially horizontal direction and the liquid containing an active ingredient is introduced into the

pouch or pouches in a substantially vertical direction.

19. A process substantially as described herein with reference to the accompanying drawings.

5


2
11
4
5
14
10
9
12
15
13
20
1
3
19
17
8
7
6
16
22
18
21
23
24
25
26
28
27
30
31
29

INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/GB 99/01138

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/70 B65B9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K B65B B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 614 076 A (RATHEMACHER JOHN W) 30 September 1986 (1986-09-30) claims; figures 1,2,6,7 ---	
A	US 4 845 926 A (DAVIS STEVEN D) 11 July 1989 (1989-07-11) column 3, line 42 - column 4, line 2 claims 12-16; figures 1-3 ---	
A	US 4 004 399 A (BORRELLO DENIS) 25 January 1977 (1977-01-25) column 6, line 8 - line 12 claims 1-12; figures 2,4 ---	
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 July 1999	20/07/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Epskamp, S

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/GB 99/01138

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 210 908 A (SAMBERG MICHAEL) 12 October 1965 (1965-10-12) column 1, line 27 - line 46 column 4, line 46 - line 51 claims 1-5; figures 1-4	
A	FR 1 068 961 A (WASSILIEF VICTOR) 2 July 1954 (1954-07-02) column 1, line 36 - column 2, line 7 column 6, line 11 - line 15 claims; figures	
A	US 4 769 974 A (DAVIS STEVEN D) 13 September 1988 (1988-09-13) claims; figures	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. ...nal Application No
PCT/GB 99/01138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4614076 A	30-09-1986	CA 1266426 A,C	06-03-1990
		EP 0202391 A	26-11-1986
US 4845926 A	11-07-1989	US 4769974 A	13-09-1988
		US 4768330 A	06-09-1988
US 4004399 A	25-01-1977	DE 2610513 A	23-09-1976
		FR 2303712 A	08-10-1976
		GB 1508704 A	26-04-1978
		JP 1051984 C	26-06-1981
		JP 51116785 A	14-10-1976
		JP 55043963 B	10-11-1980
		US 4067173 A	10-01-1978
US 3210908 A	12-10-1965	NONE	
FR 1068961 A	02-07-1954	NONE	
US 4769974 A	13-09-1988	US 4845926 A	11-07-1989